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EXAMINER	
YANG, NELSON C	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,232	BURCH ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,28-32,34,35,38-40 and 92-94* is/are pending in the application.

4a) Of the above claim(s) *1-23,41,42 and 44-91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,28-32,34,35,38-40,43 and 92-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendments submitted December 29, 2003 are acknowledged and have been entered.

2. Applicant's cancellation of claims 33, 36, and 37 is acknowledged and has been entered.

3. Claims 1-24, 28-32, 34, 35, 38-40, 43-94 are pending, of which

4. Claims 1-23, 41-42 and 44-91 were withdrawn.

Rejections Withdrawn

5. Applicant's arguments, see pages 8-9, filed December 29, 2003, with respect to the objections of the specifications have been fully considered and are persuasive. The objection of the specification and claims 36, 37 has been withdrawn.

6. Applicant's arguments, see page 9, filed December 29, 2003, with respect to claims 29, 39, and 40 under 35 U.S.C. 112have been fully considered and are persuasive. The rejection of claims 29, 39, and 40 has been withdrawn.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 24, 28-32, 34, 35, 38-40, 43, and 92-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 24 recites the limitation "wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor". However in the specification, applicants teach that the key component fragment is to be interpreted as "a portion of a molecule which *potentially* contributes to the binding affinity of that molecule for a target receptor". This renders the meaning of the phrase "key component fragment" unclear. This is also applicable to claims 93 and 94.

10. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps on how to identify one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor. In the specification, applicants only teach that a key component fragment is "a portion of a molecule which potentially contributes to the binding affinity of that molecule for a target receptor", and of identifying analogs containing key component fragments. Applicants do not teach the means of inspecting the chemical compound such that only that portion of the molecule comprising the key component fragment can be and is identified. On page 12 of the paper submitted on June 26, 2003, applicants had stated that the key component fragments were essentially "a portion of a molecule which *potentially* contributes to the binding affinity of that molecule for a target receptor". However, applicants have not clarified whether any additional undisclosed steps are involved in identifying the key component fragments, rendering the claim unclear and indefinite. It has been assumed that in order to ensure that the entire key component fragment of a chemical compound was identified without performing any additional steps, the key component fragment would comprise the entire compound.

11. In claims 24, 93, and 94, it is unclear what is meant by the limitation "define the exposed key component fragments", rendering the claims indefinite. It is unclear whether applicants intend for this to mean that the monoclonal antibodies are capable of binding to the fragments, as it appears to mean in claim 24, or if they have a surface complementary to the fragments, or if they contain a region identical to the key component fragments, as it appears mean in claims 93 and 94.

12. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that teach how to generate antibodies that are able to define the exposed key component fragments. Although generating antibodies is well known in the art, it is unclear what is meant by the limitation "define the exposed key component fragment", and therefore a person of ordinary skill in the art would not be able to generate antibodies that define the exposed key component fragment, without either further clarification or additional steps teaching how to do so or both.

13. It is unclear what is meant by the term "binding affinity" in step a) of claim 24. In the specification, applicant defines binding affinity as "the strength with which the antibody binds to a binding partner". However, in step a), applicant is discussing the binding affinity of a chemical compound, rendering it unclear how binding affinity would apply to the chemical compound. Furthermore it is unclear how the strength with which an antibody binds to a binding partner is determined, whether it is by measuring the dissociation constant, by measuring the strength of the bonds between the antibody and a binding partner, by measuring the specificity of the antibody, or by some other undisclosed method. This is also applicable to claims 93 and 94.

Currently the strength of the binding affinity is interpreted to be based on the dissociation rate constant.

14. It is unclear if claim 24 is directed toward a method of identifying one or more compounds of interest having a binding affinity for a target receptor or toward a method of identifying one or more compounds of interest having a binding affinity for a monoclonal antibody exhibiting the "strongest binding" toward the key component fragments of the compounds of interest. Furthermore, it is unclear whether the strongest binding is only relative to the monoclonal antibodies generated, or if it refers to all monoclonal antibodies, even those not generated by the analog-carrier conjugates. This is also applicable to the use of the phrase "strongest binding" in claim 28. Currently, "strongest binding" is interpreted as greatest binding affinity.

15. The term "strongest" in claim 24 is a relative term which renders the claim indefinite. The term "strongest" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what is meant strongest binding, whether it is in reference to the strength of the bond between the antibody and receptor, or in reference to the dissociation constant, or in reference to the specificity or reactivity of the antibody for the receptor. Furthermore, applicant does not clearly define what would constitute the strongest binding in the specification, rendering the claim indefinite.

16. With respect to claims 93 and 94, it is not clear what is meant by the term "most specific", and support defining the term "most specific" cannot be found in the specification, rendering the claims indefinite. Applicant is asked to clarify what basis of measurement is used

to determine monoclonal antibodies "most specific" for the key component fragments, whether it is dissociation constants, binding equilibrium constants, bond strength, percent bound to target fragment, or by some other means of measurement that has not been disclosed. Furthermore, it is unclear whether this is an individual assessment (an antibody is most specific for a particular fragment) or a competitive assessment (of all the antibodies, a particular antibody is most specific for a particular fragment). Currently, "most specific" is interpreted as having the same meaning as "strongest binding", which has been discussed above.

17. Claim 93 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps detailing how applicant plans to determine which antibodies are most specific. While applicant teaches the use of assays in step d), which would presumably determine whether the antibodies are specific for a fragment by whether binding occurs during the assay, it is unclear how applicants plan to determine which antibody is most specific for a particular fragment. It is unclear whether applicants plan to base this determination using percent fluorescence for each antibody, or if applicants plan to utilize competitive assays, or if applicants plan to measure the dissociation constant, or if some other means of determination is to be used. This is also applicable to claim 94.

18. The remaining claims are indefinite due to their dependence on an indefinite claim.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 24, 28, 31, 32, 34, 36-40, 43, and 92-94 are rejected under 35 U.S.C. 102(e) as being anticipated by Kauvar et al [US 5,674,688] in view of Kutscher et al [US 5,942,493].

With respect to claims 24, 93-94, Kauvar et al teaches identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor (claim 1), coupling one or more analogs of the compounds to a carrier molecule to construct one or more analog-carrier conjugates (column 8, lines 25-55), utilizing the analog-carrier conjugates to generate a panel of monoclonal antibodies *in vitro* and *in vivo* (column 8-9, lines 1-21 and example 1), assaying the monoclonal antibodies to determine specificity (claim 11), immobilizing the monoclonal antibodies on a support (column 7-8, lines 41-45 and preparation A), conducting a series of in-vitro assays utilizing said immobilized antibodies to screen one or more compounds of interest (columns 9-11, examples 1-2). Kauvar et al further teaches identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor (claim 1), coupling one or more analogs of the compounds to a carrier molecule to construct one or more analog-carrier conjugates (column 8, lines 25-55), utilizing two or more analog-carrier conjugates to generate a panel of monoclonal antibodies (column 8-9, example 1, claims 1, 2, 11-12), assaying the monoclonal antibodies to determine specificity and binding affinities (column 2, lines 1-11, 21-

51, claim 11), immobilizing the monoclonal antibodies on a support (column 7-8, lines 41-45 and preparation A), conducting a series of in-vitro assays utilizing said immobilized antibodies to screen one or more compounds of interest (columns 9-11, examples 1-2). Although Kauvar et al do not specifically teach immobilizing monoclonal antibodies with the strongest binding or being the most specific for a specific fragment, a person of ordinary skill in the art would realize that of the analytes being screened, one of the antibodies immobilized would have the strongest binding or be most specific for that particular analyte. Kauvar et al do not specifically teach the measurement of the dissociation constant. Kutscher et al, however, teach that the binding affinities, which Kauvar et al do teach, can be calculated as the dissociation constant (columns 42-43, example 48), in order to determine maximum binding. Therefore it would have been obvious in the method of Kauvar et al, to measure the dissociation constant as taught by Kutscher et al, in order to determine the binding affinities, in order to determine maximum binding.

21. With respect to claim 28, monoclonal antibodies for each analog-carrier conjugate exhibiting the strongest binding are included in a panel (column 5, line 46 – column 7, line 28).

22. The method of Kauvar as disclosed above fails to recite the specific feature of generating monoclonal antibodies with a dissociation constant in the range of 0.01 nM to 10 nM. However, it would have been obvious for a person of ordinary skill in the art to generate conjugates with dissociation constants within this particular range to achieve monoclonal antibodies having the strongest binding, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to

discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claim 29 are for any particular purpose or to solve any stated problem and the prior art discloses that additional methods for conducting assays designed to detect and measure binding are used to create the SC profiles, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the dissociation constants of the monoclonal antibodies in the method disclosed by Kauvar et al by normal optimization procedures known in the art.

23. With respect to claims 31, the monoclonal antibodies can be generated *in vitro* (column 7, line 63-67 and column 8-9, lines 1-21 and example 1).

24. With respect to claim 32, the analog-carrier conjugates are constructed using an amino functional group (column 8, example 1).

25. With respect to claim 34, the carrier molecule is Keyhole Limpet Hemocyanin (KLH) (column 7, line 63 – column 8, line 21).

26. With respect to claim 38, atrazine, simazine prometon are organic compounds (column 8, table 1).

27. With respect to claim 39 and 40, the method of Kauvar is used to detect altrazine (215.69), which has a molecular weight less than 500 g/mole (column 8, table 1).

28. With respect to claim 43, the panel of Kauvar is composed of 2-20 monoclonal antibodies (column 8, example 1, column 9, lines 40-42, claim s1, 20).

29. With respect to claim 92, the compounds of interest are synthetic products (herbicides) (column 8, table 1)

30. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al [US 5,674,688] in light of Harlow [Antibodies: A Laboratory Manual].

The method disclosed by Kauvar does not specify whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, but he does disclose an embodiment in which antibodies are generated *in vitro* (column 7, line 63-67 and column 8-9, lines 1-21 and example 1). However, methods of generating monoclonal antibodies *in vivo* would be well known to a person of ordinary skill in the art as well, as taught by Harlow.

31. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al [US 5,939,272] in view of Buechler et al [US 5,939,272]. The method of Kauvar fails to disclose the use of chemical compounds that exhibit PDEIV inhibitor or opiate activity. Buechler suggests a chemical compound that exhibits opiate activity (opiates), for the purpose of creating a drugs of abuse panel (column 30, line 2, column 38, example 11). Therefore it would have been obvious for a person of ordinary skill in the art to use the method of Kauvar to test for chemical counds that exhibit opiate activity.

32. Claims 24, 28-32, 34, 35, 38-40, 43, 92-94 are rejected under 35 U.S.C. 102(b) as being anticipated by Cucumel et al [Cucumel et al, Anti-idiotrypic antibodies: a useful alternative for

studying the biochemical expression of μ/δ opioid binding sites in mammalian brain, 1995, J Neuroimm, 62, 183-195] in view of Buechler et al [US 5,939,272].

With respect to claims 24, 93, and 94, Cucumel et al disclose a method of identifying a compound which have binding affinity for a target receptor comprising identifying the antiidiotypic monoclonal antibodies opiate epitope binding region (p.186, col.2, pg.3) and making analogs of these epitope binding region (p.183, col.2, pg.2), conjugating to an immunogenic form to KLH as carrier (p.184, col.1, pg. 3 – col.2, pg.1) and administering into animal to generate a pool of antibodies (p. 184, col.2, pg. 4 – p. 191, col.1). Cucumel et al do not teach the step of conducting a series of in-vitro assays utilizing the immobilized monoclonal antibodies to screen one or more compounds of interest. Buechler et al, however, do teach the step of conducting in-vitro assays utilizing immobilized monoclonal antibodies, teaching that "ligand-receptor assays are generally useful for the in vitro determination of the presence and concentration of ligands in body fluids, food products, animal fluids, and environmental samples. For example, the determination of specific hormones, proteins, therapeutic drugs, and toxic drugs in human blood or urine has significantly improved the medical diagnosis of the human condition. Furthermore, in many situations, such assays need to be simple enough to be performed and interpreted by non-technical users" (column 1, lines 53-64). Therefore it would have been obvious in the method of Cucumel et al, to conduct in-vitro assays utilizing the immobilized antibodies, in order to produce assays simple enough to be performed and interpreted by non-technical users, and to further improve the medical diagnosis of the human condition.

33. With respect to claims 28 and 29, the monoclonal antibodies generated are tested for their dissociation constant, and those exhibiting the strongest binding are included in a panel (p.186, col.2, pg.1-4). The claimed dissociation constant of the analogs is a property considered inherent to the prior art analog. Furthermore, it would have been obvious for a person of ordinary skill in the art to generate conjugates with a dissociation constant within this particular range of about 0.01nM –10nM, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claims 29 are for any particular purpose or solve any stated problem and the prior art teaches the use of analogs with dissociation constants, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by Cucumel et al by normal optimization procedures known in the art.

34. With respect to claims 30, Buechler does not specify whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, but he does disclose an embodiment in which antibodies are generated *in vivo* (column 38, lines 35-40). Furthermore, methods of generating monoclonal

antibodies *in vivo* would be well known to a person of ordinary skill in the art as well, as taught by Harlow [Antibodies: A Laboratory Manual].

35. With respect to claim 31, although Cucumel et al do not specifically indicate whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, an embodiment in which antibodies are generated *in vitro* is disclosed (p.185, col.1, pg.2 – p.186, col.2, pg.2). Furthermore, methods of generating monoclonal antibodies *in vitro* would be well known to a person of ordinary skill in the art as well [Keiser, *Monoclonal antibodies against human low density lipoprotein*, 1990, Matrix, 10, pg 97].

36. With respect to claim 32, Buechler discloses various embodiments of the invention involving analog-carrier conjugates with amino functional groups (columns 39-40, example 13, column 45, example 19).

37. With respect to claim 34, Cucumel et al teach the use of Keyhole Limpet Hemocyanin as a carrier (p.184, col.1, pg. 3 – col.2, pg.1).

38. With respect to claims 35, 38, Cucumel et al teach that the compounds are organic molecules that exhibit opiate activity (p.185, col.2, pg.3-4).

39. With respect to claims 39-40, the compounds have a molecular weight of less than approximately 500 g/mole (p. 191).

40. With respect to claim 43, the panel of antibodies is comprised of 2-3 monoclonal antibodies (column 38, lines 22-30 of Buechler et al, p. 187-189 of Cucumel et al)

41. With respect to claim 92, Buechler suggests synthetic products such as therapeutic drugs and toxic drugs (column 1, line 55-58) as examples of compounds of interest for *in vitro* screening.

42. Claims 24, 28-32, 34, 35, 38-40, 43, 92-94 are rejected under 35 U.S.C. 102(b) as being anticipated by Chamat et al [Chamat et al, The immune response towards β-adrenergic ligands and their receptors VI. Idiotypy of monoclonal anti-alprenolol antibodies, 1986, J Imm, 136(10), 3805-3811].

With respect to claims 24, 93, and 94, Chamat et al disclose a method of identifying a compound which has binding affinity for a target receptor comprising identifying the antiidiotypic antibodies beta adrenergic ligand binding region and making analogs of these epitope binding region, conjugating to an immunogenic form to KLH as carrier and administering into an animal to generate a pool of antibodies (p.3805, col.2 – 3809, col.2). Chamat et al do not teach the step of conducting a series of in-vitro assays utilizing the immobilized monoclonal antibodies to screen one or more compounds of interest. Buechler et al, however, do teach the step of conducting in-vitro assays utilizing immobilized monoclonal antibodies, teaching that "ligand-receptor assays are generally useful for the in vitro determination of the presence and concentration of ligands in body fluids, food products, animal fluids, and environmental samples. For example, the determination of specific hormones, proteins, therapeutic drugs, and toxic drugs in human blood or urine has significantly improved the medical diagnosis of the human condition. Furthermore, in many situations, such assays need to be simple enough to be performed and interpreted by non-technical users" (column 1, lines 53-64). Therefore it would have been obvious in the method of Chamat et al, to conduct in-vitro assays utilizing the immobilized antibodies, in order to produce assays simple enough to be performed and interpreted by non-technical users, and to further improve the medical diagnosis of the human condition.

43. With respect to claims 28 and 29, the monoclonal antibodies generated are tested for their dissociation constant, and those exhibiting the strongest binding are included in a panel (p.186, col.2, pg.1-4). The claimed dissociation constant of the analogs is a property considered inherent to the prior art analog. Furthermore, it would have been obvious for a person of ordinary skill in the art to generate conjugates with a dissociation constant within this particular range of about 0.01nM –10nM, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claims 29 are for any particular purpose or solve any stated problem and the prior art teaches the use of analogs with dissociation constants, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by Chamat et al by normal optimization procedures known in the art.

44. With respect to claims 30, Buechler does not specify whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, but he does disclose an embodiment in which antibodies are generated *in vivo* (column 38, lines 35-40). Furthermore, methods of generating monoclonal

antibodies *in vivo* would be well known to a person of ordinary skill in the art as well, as taught by Harlow [Antibodies: A Laboratory Manual].

45. With respect to claim 31, although Chamat et al do not specifically indicate whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, an embodiment in which antibodies are generated *in vitro* is disclosed (p.185, col.1, pg.2 – p.186, col.2, pg.2). Furthermore, methods of generating monoclonal antibodies *in vitro* would be well known to a person of ordinary skill in the art as well [Keiser, *Monoclonal antibodies against human low density lipoprotein*, 1990, Matrix, 10, pg 97].

46. With respect to claim 32, Buechler discloses various embodiments of the invention involving analog-carrier conjugates with amino functional groups (columns 39-40, example 13, column 45, example 19).

47. With respect to claim 34, Keyhole Limpet Hemocyanin is used as a carrier molecule (p.3805, col. 2, pg.4-5).

48. With respect to claim 35, Buechler suggests a chemical compound that exhibits opiate activity (opiates) (column 30, line 2).

49. With respect to claim 38, Buechler suggests one or more chemical compounds that are organic molecules (ovulatory steroids) (column 29, lines 65-67).

50. With respect to claims 39 and 40, Buechler discloses an embodiment of the invention using estrone-3-glucuronide (11.2 mg, 25μM) as the chemical compound, which has a molecular weight of less than 500 g/mole (column 32, lines 49-57).

51. With respect to claim 43, a panel of 2-3 monoclonal antibodies is taught (p.3806, col.2, pg.4 of Chamat et al, column 38, lines 22-30 of Buechler et al).

52. With respect to claim 92, Buechler suggests synthetic products such as therapeutic drugs and toxic drugs (column 1, line 55-58) as examples of compounds of interest for *in vitro* screening.

Response to Arguments

53. With respect to applicant's arguments that profiles of reactivity and strongest binding are not the same on page 11 and 20, it was originally assumed that the determination of strongest binding was related to binding affinity, as interpreted by applicant's definition of affinity as "the strength with which the antibody binds to a binding partner" in the specification. Since Kauvar et al taught that the profile of reactivity was based on the cross reactivity, or affinity an antibody had for different analytes (column 2, lines 1-11), it was assumed that a person of ordinary skill in the art would be able to readily determine the antibody with the strongest binding for a particular fragment by observing the profiles or reactivity. Furthermore, applicants had stated previously on page 12 of the paper filed on June 26, 2003 that determining the binding affinity was readily understood by one skilled in the art. In light of applicant's arguments, however, the rejection of claims 24, 28, 31, 32, 34, 36-40, 43, and 92-94 under 35 U.S.C. 102(e) is withdrawn. Applicants are asked to further clarify what is meant by "binding affinity" and by "strongest binding", as discussed above.

54. With respect to applicant's arguments regarding the identification of key component fragments of a compound having a binding affinity for a target receptor on pages 11-12, and 15, applicants are asked to clarify how the key components fragments would be identified, as applicants fail to detail how this process would occur, rendering it unclear how a person of ordinary skill in the art would identify the key component fragments.

55. With respect to applicant's arguments regarding the limitation on defining the exposed key component fragments on pages 12 and 15, applicants are asked to further clarify what is meant by defining a key component fragment, as the phrase appears to have contradicting meanings in claims 24, 93, and 94 as discussed above.

56. With respect to applicant's arguments that determining specificity is not the same as determining strongest binding on page 12, in light of the arguments, applicants are asked to clarify what would constitute strongest binding. In addition, since Kauvar et al teach the immobilization of all the monoclonal antibodies on a support, this would by necessity include the antibodies having the strongest binding for a key component fragment, regardless of whether the strongest binding antibodies have been determined or not.

57. With respect to applicant's arguments that profiles of reactivity of antibodies and determining antibodies most specific for the key component fragments on page 14, it was assumed that determining antibodies most specific for a key component fragments would be based upon observing their specificities, which in turn would be based upon their binding affinity. Since Kauvar et al taught that the profile of reactivity was based on the cross reactivity, or affinity an antibody had for different analytes (column 2, lines 1-11), it was assumed that a person of ordinary skill in the art would be capable of determining the antibodies most specific for the key component fragments simply by looking at the profiles of reactivity. In light of applicant's arguments on page 16 as well as page 14, applicants are asked to clarify the steps involved in determining antibodies most specific for the key component fragments, as discussed above.

58. With respect to applicant's arguments on page 16 and 19, regarding "specificity" and "most specific", and that Kauvar et al only teach that the specificity is different for each monoclonal antibody, with the differences used as a means of identifying the analytes, with no teaching of most specific binding, it was originally assumed that most specific binding for a particular fragment was based off of the specificity of each monoclonal antibody for the fragment. A person of ordinary skill in the art would therefore be able to determine the most specific by observing the various specificities of the antibodies for a particular fragment. In light of applicant's arguments, however, applicants are asked to clarify what is meant by most specific, as discussed above.

59. With respect to applicant's arguments regarding immobilization of antibodies most specific for the key component fragments on a support, this argument is not found persuasive. Since Kauvar et al teach the immobilization of all the monoclonal antibodies on a support, this would by necessity include the antibodies most specific for a key component fragments.

60. With respect to applicants arguments on page 17 that the claims of the present invention provide a method for identifying compounds of interest which have binding affinity for a target receptor, not by binding the compounds of interest to the receptor itself. This argument is not found persuasive, as applicant specifically states the step of conducting a series of in-vitro assays utilizing said immobilized monoclonal antibodies, which is not precluded from being a target receptor, to screen one or more compounds of interest.

61. With respect to applicant's argument on page 17, regarding the Fc fragment of mouse IgG, the argument has been found persuasive. However, Buechler et al do teach the use of monoclonal antibodies (column 33, example 4 and column 37, example 10).

62. With respect to applicant's arguments on page 18, the argument that the step of utilizing analog-carrier conjugates for generating monoclonal antibodies in vivo or in vitro cannot be found in Buechler et al has been found persuasive.

63. With respect to applicant's arguments on page 19 regarding dissociation constants, Buechler et al teach the measurement of equilibrium binding constant, which would require knowledge of the dissociation constant. However, examiner agrees that Buechler et al do not explicitly teach the measurement of the dissociation constant, although it would have been obvious for a person of ordinary skill in the art to determine the dissociation constant. With respect to the remainder of the arguments on page 19 regarding the dissociation constant, it is unclear whether applicants are arguing that there are additional steps between measuring the dissociation constants and determining the antibodies exhibiting the strongest binding, if Buechler et al only measured the dissociation constants antibodies not exhibiting the strongest binding, if measuring the dissociation constants is not sufficient for a person of ordinary skill in the art to determine antibodies exhibiting the strongest binding, or if something entirely different is meant. As a result, applicants are asked to clarify what is meant by strongest binding, whether it is related to binding affinity and measuring dissociation constants, and if so, how it is related, as discussed above.

64. With respect to claim 20, applicant argues that Kauvar et al do not teach the steps of determining and immobilizing antibodies with the strongest binding. It was originally assumed that the determination of strongest binding was related to binding affinity, as interpreted by applicant's definition of affinity as "the strength with which the antibody binds to a binding partner" in the specification. Since Kauvar et al taught that the profile of reactivity was based on

the cross reactivity, or affinity an antibody had for different analytes (column 2, lines 1-11), it was assumed that a person of ordinary skill in the art would be able to readily determine the antibody with the strongest binding for a particular fragment by observing the profiles or reactivity. As applicant has stated, Kauvar et al teach the contacting of an unknown sample with at least two antibodies, each of which is reactive to some differing degree with members of a class of suspected analytes. Thus, this would mean that each antibody would have different reactivity, or affinity, to each of the analytes, of which one antibody would have the strongest binding for a particular analyte. However, in light of applicants arguments, it is not longer clear if "strongest binding" is necessarily related to "binding affinity", and applicant is asked to further clarify their position, as discussed above.

65. Applicant's arguments, see pages 19-25, filed December 29, 2003, with respect to the rejection(s)of claim(s) 29, 30, 35 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as discussed above.

66. With respect to applicant's arguments, applicants appear to argue that the claims depend from allowable claims, the discussion of which has been discussed above, and that the additional references cited do not cure the deficiencies found in the parent claims.

Conclusion

67. No claims are allowed.

68. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

69. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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03/08/04